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EXAMINER	
BAUGHMAN, MOLLY E	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/767,249	STUELPNAGEL ET AL.	
	Examiner	Art Unit	
	Molly E. Baughman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's arguments, in the reply filed 9/1/2006, with respect to the rejection(s) of claim(s) 29, 30, 34, 38-45 under 35 U.S.C. 102(b), claims 29, 34-38, 40-45, and 48-51 under 35 U.S.C. 102(e), and claims 30-47 under 35 U.S.C. 103 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Landegren (US 5,618,701) and Ishikawa et al. (US 5,888,834).

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 29, 30, 33, 38, 39, 41-44, 48, and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Landegren (US 5,618,701).

Regarding claim 29, Landegren describes a method of processing nucleic acid (DNA or RNA) samples for analysis by binding nucleic acid species from samples to each solid phase members of a plurality of solid phase members (i.e. multipronged solid supports) (column 2, lines 11-12, 31-37). The bound nucleic acid species is processed by introducing the solid phase members into a second or sets of receptacles (column 2, lines 40-42). In one embodiment, the solid phase members are prongs or pins extending from the surface of a plate member. In other embodiments, the manifold is

comb-like, or is defined surface areas of a plate means adapted to cooperate with respective areas (e.g..recesses) in a second plate means to define a plurality of reaction volumes therewith (column 3, lines 4-19). The solid phase members may have a substantially expanded surface area, permitted increase surface loading, by coating the surfaces with porous particles (column 3 , lines 45-48).

Regarding claims 30, 33, and 41-44, Landegren describes the solid phase surface being a molecule or a group capable of interacting with a nucleic acid species (column 3, lines 20-24). In one embodiment, a DNA fragment is attached to the manifold teeth, and dipped into the well comprising the reaction solution for PCR. The various primers can be labeled or the dNTPs' use in the subsequent extension reaction steps are labeled (column 6, lines 1-16). He also discusses the use of different labels (e.g. colored or fluorescent tag), which can be analyzed in an automatic fluorescent reader (column 6, lines 11-16 and column 7, lines 1-3).

Regarding claims 38, and 39 Landegren describes a support comprising a plurality of avidin conjugated SEPHAROSE particles on each ball-pin projection coated with a 32P-labelled oligonucleotide, 5'-modified with biotin, indicated that each prong of the support could bind in the order of 20pmol of biotinylated oligonucleotides (column 7, lines 63-67). Landegren also describes the use of avidin-coupled beads coated onto the teeth of a comb-like polystyrene manifold in example 2 (column 8, lines 1-6).

Regarding claims 48-49, Landegren discuss that solid phase may have a certain number of prongs (i.e. 96 prongs) adapted to fit into the wells of a 96well microtiter plate (column 3, lines 6-8).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 31-32, 34-37, 40, and 45-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landegren (US 5,618,701) as applied to claims 29, 30, 33, 38, 39, 41-44, 48, and 49 above, and further in view of Fodor et al. (U.S. 5,800,922).

The teachings of Landegren are discussed above, but do not discuss nucleic acids comprising single nucleotide polymorphisms, wherein they are obtained by a multiplex PCR reaction (claims 31-32). He does not discuss a method wherein the prongs, pins or comb-like element's surface areas are coated with bioactive agents selected from the group consisting of peptides, peptide structural analogs, saccarides,

fatty acids, steroids, purines and pyrimidines (claim 34). He does not discuss the array locations comprising from 10,000,000 to 2,000,000,000 bioactive agents per square centimeter (claim 35), 100,000 to 10,000,000 bioactive agents per square centimeter (claim 36), or 10,000 to 100,000 bioactive agents per square centimeter (claim 37). He does not discuss the method wherein the target analytes comprise decoder-binding ligands (claim 40). He does not discuss a method further comprising quantitating differences in concentrations of the target analytes (claim 45), wherein the target analytes are mRNA (claim 46), and wherein the mRNA is quantitated in the presence of total cellular mRNA (claim 47).

Regarding claims 31-32, and 34, Fodor et al. disclose a method of producing a substrate having a plurality of positionally distinguishable sequence specific reagents, wherein the reagents could be polynucleotides, polymers, carbohydrates, polypeptides, etc. (page 2, lines 34-67, and page 6-7, lines 63-67; 1-5). The methods can also be coupled to a polymerase chain reaction (page 27, lines 17-19, and page 58, lines 23-26), wherein specific reagents (probes) can be used to detect one or more mismatched bases in a fluorescently labeled target (page 69, lines 17-67, page 4, lines 45-64).

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to detect mismatched bases (i.e. single nucleotide polymorphisms) within a fluorescently labeled target, or detect polymers, carbohydrates, or polypeptides as taught by Fodor et al. to the method of dipping an array, containing a plurality bioactive agents, into a second substrate of target analytes, as taught by Landegren. The skilled artisan would have had a reasonable expectation of success in adding the

detection of SNPs in target nucleic acids to the method of Landegren. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed detection of SNPs in target nucleic acids, polymers, carbohydrates, or polypeptides therein.

Regarding claims 35-37, Fodor et al. disclose a method of generating the desired repertoire of oligonucleotide probes on a substrate, wherein the densities could range from 5 regions/cm^2 to an excess of one million regions/ cm^2 (page 20, lines 13-37).

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to apply the varying densities of bioactive agents at array locations by Fodor et al. to the method of dipping an array, containing a plurality bioactive agents, into a second substrate of target analytes, as taught by Landegren. The skilled artisan would have had a reasonable expectation of success in adding the various bioactive agent densities at array locations to the method of Landegren. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the various bioactive agent densities at array locations therein.

Regarding claim 40, Fodor et al. disclose the use of microspheres (beads) containing a plurality of coded substrates to indicate the sequence specificity of said reagent (page 4, lines 1-4 and page 45-46). They also disclose the use of using different labels to detect each target simultaneously, wherein one target could be labeled with a green fluorescent label and a second target a red fluorescent label. A wide variety of fluorescers may be employed (i.e. a chromagen), and can be detected

by analyzing the differences in optical signals (page 52-53). In a different labeling application, coding information can be incorporated on molecules such as nucleic acids, which can be amplified through PCR, and then later decoded (page 58, lines 11-44).

One of ordinary skill in the art would have been motivated to modify the method of Landegren to use target analytes comprising decoder binding ligands because the benefits of incorporating coding information into target molecules was shown by Fodor et al. The skilled artisan would have had a reasonable expectation of success in using target analytes comprising decoder-binding ligands in the method of Landegren. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed decoder binding ligands therein.

Regarding claims 45-47, Fodor et al. disclose characterizing various samples by testing their mRNA sequence intent (page 29, lines 33-36, and 42-46). Furthermore, they discuss defining the pattern of expression of mRNA, in comparison to other types of RNA, wherein different levels of RNA may be found in correlation to the developmental stage of the cell (page 30, lines 10-20).

One of ordinary skill in the art would have been motivated to modify the method of Landegren to quantitate the differences in levels of specific mRNA in the presence of total cellular mRNA because the benefits of quantitating various types of mRNA was shown by Fodor et al. The skilled artisan would have had a reasonable expectation of success in adding the quantification of specific mRNA levels in the method of Landegren. It would have been *prima facie* obvious to one of ordinary skill in the art at

the time of the invention to carry out the claimed methods and use the claimed quantification of specific mRNA levels therein.

7. Claims 29-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishikawa et al. (US 5,888,834), in view of Fodor et al. (U.S. 5,800,922).

Ishikawa et al. describe a method of using a dipstick type solid phase that can be inserted into a well type solid phase (see figures 1, 4, and 6) in an immunoassay. The solid phases are formed in such a shape that enables insertion of the dipstick type solid phase into the well type solid phase to combine them (column 6, lines 57-58). In the method, a receptor is coated on the dipstick type solid phase, and an antigen bound with a label is in a test solution in the well below the dipstick (column 11, lines 33-41). In example 2 (column 17), they describe the dipstick being coated with a receptor substance, while the well type solid phase contained a labeled immune complex in solution. The dipstick solid phase was inserted into the well type solid phase, wherein the immune complex became bound to the receptor coated on the dipstick solid phase. The fluorescent intensity created from the bound target was measured with a spectofluorometer.

Ishikawa et al. do not discuss a method wherein the dipstick type solid phase comprises a plurality of different array locations, comprising a plurality of discrete sites, comprising different bioactive agents, nor do they discuss the wells containing sample solutions of a plurality of different target analytes (claim 29). They do not discuss the method wherein the target analytes are nucleic acids, which comprise single nucleotide

polymorphisms obtained by multiplex PCR (claims 30-32). They do not discuss the method wherein the nucleic acids are labeled with fluorochromes during PCR amplification (claim 33). They do not discuss a method wherein the bioactive agents are selected from the group consisting of peptides, peptide structural analogs, saccarides, fatty acids, steroids, purines and pyrimidines (claim 34). They do not discuss array locations comprising from 10,000,000 to 2,000,000,000 bioactive agents per square centimeter (claim 35), 100,000 to 10,000,000 bioactive agents per square centimeter (claim 36), or 10,000 to 100,000 bioactive agents per square centimeter (claim 37). They do not discuss a method wherein the bioactive agents are attached to microspheres and the microspheres are associated with the array locations (claim 39). They not discuss the method wherein the target analytes comprise decoder-binding ligands (claim 40). They do not discuss further quantitating differences in concentrations of target analytes (claim 45), wherein the target analytes are mRNA (claim 46), and wherein the mRNA is quantitated in the presence of total cellular mRNA (claim 47).

Regarding claims 29-34, Fodor et al. disclose a method of producing a substrate having a plurality of positionally distinguishable sequence specific reagents, wherein the reagents could be polynucleotides, polymers, carbohydrates, polypeptides, etc. (page 2, lines 34-67, and page 6-7, lines 63-67; 1-5). The methods can also be coupled to a polymerase chain reaction (page 27, lines 17-19, and page 58, lines 23-26), wherein specific reagents (probes) can be used to detect one or more mismatched bases in a fluorescently labeled target (page 69, lines 17-67, page 4, lines 45-64).

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to add a substrate comprising a plurality of array locations, comprising a plurality of different bioactive agents for detecting a plurality of target analytes, wherein the method is used to detect mismatched bases (i.e. single nucleotide polymorphisms) within a fluorescently labeled target, or to detect polymers, carbohydrates, or polypeptides as taught by Fodor et al. to the method of dipping an array coated with a bioactive agent, into a second substrate comprising a target analyte, as taught by Ishikawa et al. The skilled artisan would have had a reasonable expectation of success in adding the plurality of array locations, bioactive agents, and target analytes, and further add the detection of SNPs in target nucleic acids, or the detection of polymers, carbohydrates, or polypeptides to the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed plurality of array locations, bioactive agents, and target analytes and the detection of SNPs in target nucleic acids, polymers, carbohydrates, or polypeptides therein.

Regarding claims 35-37, Fodor et al. disclose a method of generating the desired repertoire of oligonucleotide probes on a substrate, wherein the densities could range from 5 regions/cm^2 to an excess of one million regions/ cm^2 (page 20, lines 13-37).

It would have been obvious to one of ordinary skill in the art at the time of the claimed invention to apply the varying densities of bioactive agents at array locations by Fodor et al. to the method of dipping an array coated with a bioactive agent, into a second substrate comprising a target analyte, as taught by Ishikawa et al. The skilled

artisan would have had a reasonable expectation of success in adding the various bioactive agent densities at array locations onto the dipstick solid phase in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the various bioactive agent densities at array locations therein.

Regarding claims 39-40, Fodor et al. disclose the use of microspheres (beads) containing a plurality of coded substrates to indicate the sequence specificity of said reagent (page 4, lines 1-4 and page 45-46). They also disclose the use of using different labels to detect each target simultaneously, wherein one target could be labeled with a green fluorescent label and a second target a red fluorescent label. A wide variety of fluorescers may be employed (i.e. a chromagen), and can be detected by analyzing the differences in optical signals (page 52-53). In a different labeling application, coding information can be incorporated on molecules such as nucleic acids, which can be amplified through PCR, and then later decoded (page 58, lines 11-44).

One of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to use bioactive agents attached to microspheres associated with the array locations and target analytes comprising decoder binding ligands because the benefits of using microspheres (beads) containing a plurality of coded substrates and incorporating coding information into target molecules was shown by Fodor et al. The skilled artisan would have had a reasonable expectation of success in using microspheres (beads) containing a plurality of coded substrates and target analytes comprising decoder-binding ligands in the method of Ishikawa et al. It would have been

prima facie obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed microspheres and decoder binding ligands therein.

Regarding claims 45-47, Fodor et al. disclose characterizing various samples by testing their mRNA sequence intent (page 29, lines 33-36, and 42-46). Furthermore, they discuss defining the pattern of expression of mRNA, in comparison to other types of RNA, wherein different levels of RNA may be found in correlation to the developmental stage of the cell (page 30, lines 10-20).

One of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to quantitate the differences in levels of specific mRNA in the presence of total cellular mRNA because the benefits of quantitating various types of mRNA was shown by Fodor et al. The skilled artisan would have had a reasonable expectation of success in adding the quantification of specific mRNA levels in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed quantification of specific mRNA levels therein.

8. Claims 34-37, 40, 45, and 50-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landegren (US 5,618,701) as applied to claims 29, 30, 33, 38, 39, 41-44, 48, and 49 above, and further in view of Burbaum et al (U.S. 5,876,976).

The teachings of Landegren are discussed above, but he does not discuss a method wherein the prongs, pins or comb-like element's surface areas are coated with

bioactive agents selected from the group consisting of peptides, peptide structural analogs, saccarides, fatty acids, steroids, purines and pyrimidines (claim 34). He does not discuss the array locations comprising from 10,000,000 to 2,000,000,000 bioactive agents per square centimeter (claim 35), 100,000 to 10,000,000 bioactive agents per square centimeter (claim 36), or 10,000 to 100,000 bioactive agents per square centimeter (claim 37). He does not discuss the method wherein the target analytes comprise decoder-binding ligands (claim 40). He does not discuss a method further comprising quantitating differences in concentrations of the target analytes (claim 45), wherein the target analytes are mRNA (claim 46), and wherein the mRNA is quantitated in the presence of total cellular mRNA (claim 47). He does not discuss a method wherein the plurality of assay wells comprise 384 wells (claim 50), or 1536 wells (claim 51).

Regarding claim 34, Burbaum et al. disclose a solid support coated with any desired target including: peptides, antibodies, DNA-binding proteins, oligonucleotides, etc. (page 6, lines 61-67, and pages 7-8).

One of ordinary skill in the art would have been motivated to modify the method of Landegren et al. to use bioactive agents consisting of peptides, antibodies, or DNA-Binding proteins because the benefits of binding such analytes to solid supports were shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in adding bioactive agents consisting of peptides, antibodies, or DNA-Binding proteins in the method of Landegren et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the

claimed methods and use the claimed peptides, antibodies, or DNA-Binding proteins as bioactive agents therein.

Regarding claims 35-37, Burbaum et al describe the use of beads as a solid support, typically containing 10^6 binding sites per bead, and beads at preferred density of 100 to 1000 per sample volume (page 6, lines 18-21, and page 8, lines 26-44).

One of ordinary skill in the art would have been motivated to modify the method of Landegren et al. to use beads (i.e. microspheres) attached to the solid support because the benefits of using beads as solid supports were shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in adding microspheres associated with the array locations in the method of Landegren et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed microspheres therein.

Regarding claim 40, Burbaum et al disclose target analytes, in this case a library of compounds, with a chemical tag to enable the identification of the target analyte via decoding the tag (pages 9-10, lines 57-67, and 1-4 respectively).

One of ordinary skill in the art would have been motivated to modify the method of Landegren et al. to use targets comprising decoder-binding ligands because the benefits of using chemical tags for the identification of target analytes was shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in using decoder-binding ligands for the identification of target analytes in the method of Landegren et al. It would have been *prima facie* obvious to one of ordinary skill in the

art at the time of the invention to carry out the claimed methods and use the claimed target analytes comprising decoder binding ligands therein.

Regarding claim 45, Burbaum et al. disclose a method wherein target molecules can be statistically evaluated by placing a plurality of compounds in each assay container (i.e. microtiter plate), and determining the number and potency of each compound (page 10, lines 7-10 and page 8, lines 14-26). Detection is determined via signal created by bound fluorescently labeled ligands (i.e. fluorescein, rhodamine, texas red – page 8, lines 61-67) to the target molecule (page 8, lines 46-61).

One of ordinary skill in the art would have been motivated to modify the method of Landegren et al. to further quantitate the differences in concentrations of the target analytes because the benefits of statistically evaluating the number and potency of each compound was shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in further quantitating the differences in the target analytes' concentrations in the method of Landegren et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and quantitate the differences in target analyte concentrations therein.

Regarding claims 50-51, Burbaum et al disclose the invention being performed in a microtiter plate, wherein the method can be carried out in 96-well, 384-well, or 1536-well microtiter plates (page 8, lines 14-25).

One of ordinary skill in the art would have been motivated to modify the method of Landegren et al. to use assay wells comprising 384 wells or 1536 wells because the benefits of using 384 wells and 1536 wells as assay wells was shown by Burbaum et al.

The skilled artisan would have had a reasonable expectation of success in using 384 wells or 1536 wells in the method of Landegren et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed 384 assay wells or 1536 assay wells therein.

9. Claims 29, 34-39, 40-45, and 48-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishikawa et al. (US 5,888,834), in view of Burbaum et al (U.S. 5,876,976).

The teachings of Ishikawa et al. are discussed above, including the instant claims 29, 38, 39, and 41-44. Ishikawa et al. do not discuss a method wherein the dipstick type solid phase comprises a plurality of different array locations, comprising a plurality of discrete sites, comprising different bioactive agents, nor do they discuss the wells containing sample solutions of a plurality of different target analytes (claim 29). They do not discuss a method wherein the bioactive agents are selected from the group consisting of peptides, peptide structural analogs, saccarides, fatty acids, steroids, purines and pyrimidines (claim 34). They do not discuss array locations comprising from 10,000,000 to 2,000,000,000 bioactive agents per square centimeter (claim 35), 100,000 to 10,000,000 bioactive agents per square centimeter (claim 36), or 10,000 to 100,000 bioactive agents per square centimeter (claim 37). They not discuss the method wherein the target analytes comprise decoder-binding ligands (claim 40). They do not discuss further quantitating differences in concentrations of target analytes (claim 45). They do not discuss a method wherein the plurality of assay wells comprise wells

of a microtiter plate (claim 48), wherein there are 96 wells (claim 49), 384 wells (claim 50), or 1536 wells (claim 51).

The teachings of Burbaum et al. are discussed above, including the instant claims 34-37, 40, 45, and 50-51.

Regarding claim 29, Burbaum et al. disclose the use of suspendable solid supports, which can be the bottom of a microtiter plate, or polystyrene beads containing 10^6 binding sites for coating with a target molecule, and then exposed to labeled ligands (page 6, lines 18-21 and 44-47 and page 9, lines 18-27). The solid support can be coated with any desired target molecule (column 6, lines 62-67), and in one embodiment, can be combinatorial libraries (column 9, lines 48-67). The assay is investigated by individually evaluating each of the plurality of target analytes present in the wells (column 10, lines 5-19).

One of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to use a plurality of array locations comprising a plurality of bioactive agents to analyze a plurality of target analytes because the benefits of analyzing a plurality of target analytes by suspending solid supports comprising a plurality of array locations comprising a plurality of target molecules was shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in using a plurality of array locations comprising a plurality of bioactive agents to analyze a plurality of target analytes in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed

methods and use the claimed plurality of array locations, bioactive agents, and target analytes therein.

Regarding claim 34, one of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to use bioactive agents consisting of peptides, antibodies, or DNA-Binding proteins because the benefits of binding such analytes to solid supports were shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in adding bioactive agents consisting of peptides, antibodies, or DNA-Binding proteins in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed peptides, antibodies, or DNA-Binding proteins as bioactive agents therein.

Regarding claims 35-37, one of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to use beads (i.e. microspheres) attached to the solid support because the benefits of using beads as solid supports were shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in adding microspheres associated with the array locations in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed microspheres therein.

Regarding claim 40, one of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to use targets comprising decoder binding ligands because the benefits of using chemical tags for the identification of target analytes were

shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in using decoder-binding ligands for the identification of target analytes in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed target analytes comprising decoder binding ligands therein.

Regarding claim 45, one of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to further quantitate the differences in concentrations of the target analytes because the benefits of statistically evaluating the number and potency of each compound was shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success in further quantitating the differences in the target analytes' concentrations in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and quantitate the differences in target analyte concentrations therein.

Regarding claims 48-51, Burbaum et al disclose the invention being performed in a microtiter plate, wherein the method can be carried out in 96-well, 384-well, or 1536-well microtiter plates (page 8, lines 14-25).

One of ordinary skill in the art would have been motivated to modify the method of Ishikawa et al. to use assay wells comprising wells of a microtiter plate, or assay wells comprising 96 wells, 384 wells or 1536 wells because the benefits of using microtiter plates of 96 wells, 384 wells and 1536 wells as assay wells was shown by Burbaum et al. The skilled artisan would have had a reasonable expectation of success

in using microtiter plates of 96 wells, 384 wells or 1536 wells in the method of Ishikawa et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed 96 well, 384 well or 1536 well microtiter plates therein.

SUMMARY

10. No claims are free of the prior art.

CONCLUSIONS

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Molly E Baughman
Examiner
Art Unit 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

10/30/06